UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,591	04/02/2004	Matti Sallberg	TRIPEP.23AUS2C1	4899

20995 7590 02/27/2006

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/817,591	SALLBERG ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11.15/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-81* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-81* is/are rejected.

7)☒ Claim(s) *67-73 and 75-81* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09/15/05&08/11/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to the amendment

This is to acknowledge the amendment filed on 12/15/2005. Claims 1-35 have been canceled. New claims 66-81 have been added. Claims 36-81 are pending.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. (See line 4 on page 11).

Election/Restrictions

1. Applicant's election without traverse of Group I in the scope of HCV, read on claims 36-81 in the reply filed on 12/15/2005 is acknowledged. Claims 36-81 in the scope of HCV are considered before the examiner. Applicants are reminded to amend claims to the scope for reflecting the examination on the merits.

Claim Objections

2. Claims 67-73 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim 66. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, the claims 67-73 do not further limit the claimed subject matters in claim 66 because the claimed subject matters in those claims have much more broader scopes than that of claim 66 since the claimed DNA molecules may contain the structures beyond the limitation of SEQ ID NO: 16 in claim 66.

3. Claims 75-81 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim 74. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case,

the claims 67-73 do not further limit the claimed subject matters in claim 74because the claimed subject matters in those claims have much more broader scopes than that of claim 66 since the claimed DNA molecules may contain the structures beyond the limitation of SEQ ID NO: 16 in claim 74.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 36-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains new matters, which were not fully described in the specification and were not disclosed in the parental applications that the current application claims as priority documents in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the specific method steps cited in claims 36 and 51 that read on identifying a subject in need of an enhanced production (claim 36) or an improvement in a T cell response (claim 51) are not described in the specification of current application (except the claims 36 and 51) and in the parental applications that applicants claim as continuations of priority documents 09/929,955 or 10/104,966, which claim benefit of provisional application 60/225,767 and 60/229, 175. These affect all claims that depended on claims 36 and 51.

6. **MPEP cited in 201.07 [R-1]: A continuation is a second application for the same invention claimed in a prior nonprovisional application and filed before the original prior application becomes abandoned or patented. The continuation application may be filed under 37 CFR 1.53(b) or 1.53(d). The applicant in the continuation application must include at least one inventor named in the prior nonprovisional application. The disclosure presented in the continuation must be the same as that of the original application; i.e., the continuation should not include**

anything, which would constitute new matter if inserted in the original application. The continuation application must claim the benefit of the prior nonprovisional application under 35 U.S.C. 120 or 365(c). In the instant case, the specification only describe to administer a composition comprising hepatitis C viral antigen and ribavirin, preferably HCV NS3 and/or NS4 to an animal model, which is able to produced an enhanced humoral as well as CD4+ T cell activation. The specification of current application as well as all claimed priority documents do not have any description how each particular immune response is measured or accessed in a subject prior to be selected for using said composition comprising HCV viral antigen and ribavirin. Therefore, applicants are required to cancel the new matter in order to overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 36-39, 42-54, 67-73 and 75-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing an enhanced immune response against an HCV specific antigen NS3/NS4A encoded by SEQ ID NO: 16 by administering it intramuscularly, does not reasonably provide enablement for producing an enhanced specific immune response against a viral antigen encoded by the entire HCV genomic sequence or only a fell base pairs of SEQ ISD NO: 16, such as 12 to 20 mers consecutive nucleotides of SEQ ID NO: 16 by any administering methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

8. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would render undue experimentation (See United States v.

Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988) set forth below: 1). The nature of invention: 2). Scope of the claim; 3). Level of skill to perform the invention; 4). State of art; 5). Unpredictability in the field, 6). Number of working examples in the specification; 7). Amount of guidance provided by the specification.

9. In the instant case, the claimed invention is drawn to a method for producing an enhanced specific humoral and cellular immune responses against a specific HCV viral antigen by using a DNA immunization approach, wherein the DNA immunization composition comprising the nucleotide sequence of SEQ ID NO: 16 that encodes the particular HCV antigen NS3/NS4 polypeptide antigen in combination of ribavirin. However, the scope of the claims read on an unreasonable broad that includes the nucleotide comprising either as big as a whole HCV virus genome or few base pairs of SEQ ID NO: 16, such as 12 or 20 consecutive nucleotides of SEQ ID NO: 16 in combination with ribavirin.

10. The specification only teaches that a composition made by mixing 500 μg or 100 μg of nucleic acids encoding rNS3/4A of SEQ ID NO: 16 as a plasmid with 1 mg ribavirin (See disclosure at lines 7-18 on page 65 of specification), which is able to produce an enhanced type 1 IgG antibodies after the composition is administered into a host. The specification does not teach which 12 or 20 mers of nucleotides encoding an antigen specific epitope and how to select an epitope along a DNA molecule comprising at least 2061 base pairs set forth in SEQ ID NO: 16. The specification does not provide sufficient evidence or adequate guidance to support the broadly claimed invention.

11. State of art teaches that the DNA vaccine can be made by injecting a plasmid into a host through muscular injection. State of art also teaches that each HCV antigenic polypeptide or peptide but not the whole HCV genome is able to induce an immune response after administering into an animal. It is unpredictable whether the injection of a whole viral genome or the HCV genome into a subject will induce an enhanced immune response or produce a replicating or infectious hepatitis C viral RNA since transfecting a

subgenomic HCV into a cell line can produce infectious HCV RNA in vitro as evidenced by Lohman et al. (Science 1999, Vol. 285, pp. 110-113, see abstract) or an acute or persistent infection in vivo as evidenced by Forns et al. (PNAS 2000, Vol. 97, pp. 13318-13323, see abstract). State of art also teaches that a single nucleic acid change would change the protein that original nucleotides encodes due to the frame shift, and a single amino acid change may change the antigenicity of an antigen originally possesses as evidenced by Rudikoff et al. (Immunology 1982, Vol. 79, pp. 1979-1983, see page 1579). Therefore, it is unpredictable if only 12 consecutive nucleotides of SEQ ID NO: 16 is able to produce an antigen that still possess the original imunogenicity of the HCV NS3/4 and induce an antigen specific immune response to HCV NS3/4 antigen.

12. The level of skill in the art to perform the full scope of invention should be at the PhD level for selecting a suitable 12 to 20 mers of nucleotides and test each of the selections for the ability of inducing an enhanced immune response.

13. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164

USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

15. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

16. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 36-40, 42-55, 57-65 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-47, 51-55, 57-70, 72-80 of copending Application No. 10,719,619. Although the conflicting claims are not identical, they are not patentably distinct from each other because an HCV antigen can be broadly explained either as a nucleic acid molecule and an amino acid molecule. If the antigen in the conflict claims of co-pending application is interpreted as an nucleic acid molecule, the scopes of conflict claims are overlapping and the conflict claims are anticipated each other.

18. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 36-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Encke et al. (J. Immunol. 1998, Vol. 161, pp. 4917-4923), Tam (US Patent NO. 5,767,097A) and Hultgren et al (J. Gene. Virol. 1998, Vol. 79, pp. 2381-2391).

21. Claimed invention is drawn to a method using a DNA vaccine composition comprising a nucleotides encoding HCV antigen, preferably NS3/4 protein and ribavirin.

22. Encke et al. teach that hepatitis C virus (HCV) non-structural (NS) proteins may play an important role in virus elimination. After 3 intramuscular DNA-based immunizations that encode NS3, NS4 and NS5 in mice, all animals developed detectable antibody responses and generation of inflammatory CD4+ T-cell responses with a predominant TH1 phenotype immune response with all 3 plasmids encoding the NS3, NS4 and NS5 (See pages 4917, Fig. 2, 4921). Encke et al. do not teach to use ribavirin in combination of HCV antigen(s) to produce an enhanced immune response.

23. Tam R. teaches a method for produce an enhanced Th1 type immune response to a specific antigen by administering a composition comprising a viral antigen component with rebavirin into patients (Claims 1-9).

24. Hultgren et al. teach a method for inducing an enhanced TH-1 type cellular immune response, such as Th1 type of cytokine secretion of IL2 or INFγ (Fig. 5) and humoral antibody with HBV e Antigen (Fig. 4 and 5) and HCV NS3 or HCV core antigen (Fig. 4) with a daily dosages ranged from 0.75-1.5 mg per day after the mice were immunized with said antigens (See Methods on pages 2382-2383).

25. Therefore, on the basis of the disclosure of Encke et al. that DNA plasmids encoding HCV non-structural protein NS3-5 are able to induce predominantly Th-1 type immune response to each HCV, and disclosures by Tam R and Hulgren et al. that ribavirin favors to increase the TH1 type immune response and increase the Th-1 type cellular and humoral immune response against the targeted hepatitis viral antigens when it is used in combination with said viral antigen, it would have been obvious to one of ordinary skill in the art at the time of the invention was filled to be motivated in order to produce an enhanced Th-1 type cellular and humoral immune response, to use any HCV non-structural protein selected from NS3 to NS5 or a combination thereof in combined with ribavirin absence unexpected result.

26. Regarding to the limitation for co-administering HCV NS3 and ribavirin at one time or separately, it is only considered as a designed choice since the functions exhibited by the two kinds of drugs administrations are same. Unless Applicants provide an evidence indicating that the single administration produces more significant result than the consequently two individual administrations, the claimed invention as a whole is prima facie obvious absence unexpected result.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li
BAOQUN LI, MD
PATENT EXAMINER
02/22/2006